

REMARKS

Claims 78, 98-115, and 119-123, are pending in the present application. Claims 1-77, 79-97 and 116-118, have been canceled without prejudice or disclaimer.

Independent claim 78 is directed to "A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said biological matter and the other being below the freezing point, comprising providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the temperature of said sample by the following steps: (i) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature; (ii) further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature. Claims 98-115 and 119 depend, either

directly or indirectly, from claim 78

Claim 121 is directed to "A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said matter and the other being below the freezing point, comprising providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the temperature of said sample by the following steps: (i) (a) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature, said changing is achieved by moving the sample through a region with a temperature gradient from the initial temperature to the intermediate temperature, said sample has a leading end along the direction of movement; (b) moving the leading end of the into a region with a temperature gradient from the initial temperature to the intermediate temperature; (c) pausing the movement until seeding takes place at the leading end; and moving the sample through said region; (ii) further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the

intermediate temperature; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature, said changing is achieved by moving the sample through a region with a temperature gradient from the intermediate temperature to the final temperature.”

Claim 122 is directed to “A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said matter and the other being below the freezing point, comprising providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the temperature of said sample by the following steps: (i) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature; (ii) (a) further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature, said changing is performed by placing said sample in a region with the intermediate temperature, said region having a length along the direction of the movement of said sample and said length

is not less the length of the sample along said direction of movement; (b) moving the sample into the region with the intermediate temperature, until substantially the whole sample is within said region; (c) pausing the movement of the sample within said region until the temperature of the sample is substantially uniform throughout the sample and equals the intermediate temperature; (d) moving the sample out of said region; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature.”

Claim 123 is directed to “A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said matter and the other being below the freezing point, comprising providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the temperature of said sample by the following steps: (i) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature; (ii) further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least

one cross-section is uniform and equals the intermediate temperature, and moving the sample into a region with the intermediate temperature and subjecting the sample to the intermediate temperature in said region until the temperature of said sample in each cross-section taken perpendicularly to said direction reaches the intermediate temperature by the time it is moved out of said region; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature.”

In view of the following, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, claims 78, 98-115 and 119-123 have been rejected under 35 USC § 112, first paragraph.

The Examiner asserts that claims 78, 98-115 and 119-123 fail to comply with the written description requirement because the term “biological matter” allegedly is a broadening of the disclosure in the original specification.

Applicants respectfully traverse this rejection.

The test under 35 U.S.C. 112, first paragraph, for determining compliance with the written description requirement is whether the application clearly conveys that an Applicant has invented the subject matter which is claimed. *In re Barker*, 194 USPQ 470, 473 (CCPA 1977); MPEP 2163. Also, the Applicant must convey to the public what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything in common use or already known. MPEP § 2163. Lastly, the specification must convey that the applicant was in possession of the invention. MPEP § 2163. The Examiner

is respectfully reminded that the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an Applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 191USPQ 90, 98 (CCPA 1976).

Applicants respectfully submit that the present claims fully comply with the written description requirement. Specifically, Applicants submit that reading the present claims in view of the specification a skilled artisan would have sufficient description for the term "biological matter." As disclosed at page 4, lines 18-21 of the specification as originally filed,

A "sample" means an amount of **biological matter including** cells and/or group of cells and/or bodily fluids and/or any constituents thereof. For example, a sample may comprise semen, oocytes (ova), blood, blood cells, blood constituents, germ cells, umbilical cord blood, plasma, zygotes and embryos. See the specification at page 4, lines 18-21. (Emphasis Added).

Applicants respectfully submit that the term "biological matter" corresponds with the term sample. Additionally, Applicants note that the term "biological matter" is described as including "cells and/or group of cells and/or bodily fluids and/or any constituents thereof." See *Id.* Therefore, any "sample" is "biological matter." Further, "biological matter" includes "cells and/or group of cells and/or bodily fluids and/or any constituents thereof." Applicants note in view of the aforementioned disclosure of the specification, the recitation of the term "biological matter" would be clear to any person of skill in the art.

In view of the foregoing, Applicants submit that claims 78, 98-115 and 119-123 fully comply with the written description requirement of 35 USC § 112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

II. At page 2 of the Official Action, claims 78, and 98-115 and 119-123 have been rejected under 35 USC § 103 (a) as being unpatentable over US Patent No. 5,873,254.

The Examiner maintains the rejection set forth in the previous Official Action dated May 14, 2007. Specifically, the Examiner asserts that the '254 patent does not describe the size of the sample and that the generic description is not limited with regard to the size of the sample. Additionally, the Examiner asserts that the exemplification of the size of the sample in the cited reference is "ABOUT 1 cm x 1 cm x 0.5 cm," and that the "use of the term "about" in the above exemplification "permits a variation of undefined range around this measurement at the very least to ABOUT 2mm, which is the size of the container." Lastly, the Examiner asserts that mere scaling up of a prior art process is not sufficient to patentably distinguish over prior art.

In view of the following, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, Slip Opinion No. 04-1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design

community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” (*KSR, supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

As discussed, claim 78 is directed to “A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said biological matter and the other being below the freezing point, comprising ***providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters***, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the

temperature of said sample by the following steps: (i) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature; (ii) ***further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature***; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature. (Emphasis Added). Claims 98-115 and 119 depend, either directly or indirectly, from claim 78.

Claim 121 is directed to "A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said matter and the other being below the freezing point, comprising ***providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters***, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the temperature of said sample by the following steps: (i) (a) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the

outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature, said changing is achieved by moving the sample through a region with a temperature gradient from the initial temperature to the intermediate temperature, said sample has a leading end along the direction of movement; (b) moving the leading end of the into a region with a temperature gradient from the initial temperature to the intermediate temperature; (c) pausing the movement until seeding takes place at the leading end; and moving the sample through said region; (ii) ***further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature***; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature, said changing is achieved by moving the sample through a region with a temperature gradient from the intermediate temperature to the final temperature.”

Claim 122 is directed to “A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said matter and the other being below the freezing point, comprising ***providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters***, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the

temperature of said sample by the following steps: (i) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature; (ii) (a) ***further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature***, said changing is performed by placing said sample in a region with the intermediate temperature, said region having a length along the direction of the movement of said sample and said length is not less the length of the sample along said direction of movement; (b) moving the sample into the region with the intermediate temperature, until substantially the whole sample is within said region; (c) pausing the movement of the sample within said region until the temperature of the sample is substantially uniform throughout the sample and equals the intermediate temperature; (d) moving the sample out of said region; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature.”

Claim 123 is directed to “A method for changing the temperature of a biological matter from an initial temperature via an intermediate temperature to a final temperature, one of the initial and final temperatures being above the freezing point of said matter and the other being below the freezing point, comprising ***providing said biological matter in the form of a sample whose minimal dimension in each of two mutually***

perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone, and changing the temperature of said sample by the following steps: (i) changing the temperature of the sample by subjecting it to a temperature gradient from the initial temperature to the intermediate temperature until the temperature of the sample in at least one part of the outer zone equals the intermediate temperature whilst the temperature of the sample in the inner zone is different from said intermediate temperature; (ii) ***further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature***, and moving the sample into a region with the intermediate temperature and subjecting the sample to the intermediate temperature in said region until the temperature of said sample in each cross-section taken perpendicularly to said direction reaches the intermediate temperature by the time it is moved out of said region; and (iii) changing the temperature of said sample until the majority of said sample is at the final temperature.”

In contrast the ‘254 patent describes a method of changing the temperature of a biological matter. However, the ‘254 patent does not teach or suggest ***"providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters."*** Therefore, in contrast to the methods of claims 78 and 121-123, ‘254 does not address the issue of the

temperature of the sample in its outer zone in each of its cross-sections changing quicker than that in the inner zone.

Each of the presently pending independent claims recite:

...providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone.... See claims 78 and 121-123.

Additionally, each of the presently pending independent claims recite the step of:

...further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature.... See claims 78 and 121-123.

In addition, Applicants note that as disclosed in the specification as originally filed at page 6, line 29 to page 7, line 6:

It is by virtue of the present invention that cryopreservation of large samples and of samples having a large volume, may be successfully performed. This is preferably achieved by seeing that at least in most of the sample frozen or thawed according to the method of the invention has essentially the same temperature history, as all the other parts. This is of essence for example where the intermediate temperature is of a critical nature, namely that one rate of freezing (or thawing) is preferred between the initial and intermediate temperatures, and another is preferred between the intermediate and final temperatures. See the specification at page 6, line 29 to page 7. (Emphasis Added).

Thus, the use of the presently claimed combination of temperature change stages, is non-obvious over the '254 patent because the '254 patent does not describe methods involving sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters.

Applicants respectfully submit that in contradiction to the ***essentially simultaneous*** (or at least very quick) temperature change between outer and inner zones of a small sample, ***the temperature of a large sample does not change uniformly*** when the entire sample is subjected to a temperature different than that of the sample. Therefore, the presently claimed subject matter includes bringing the sample to an intermediate temperature by first ensuring that at least a part of the outer zone of the sample is brought to the intermediate temperature whilst the inner zone or another part of the outer zone has a temperature different from the intermediate temperature, and ***then subjecting the sample to the intermediate temperature until the temperature in at least one cross-section, and preferably in all cross-sections perpendicular to the direction of movement of the sample, is uniform.*** Applicants emphasize that only after the uniformity is achieved, step (iii), i.e., "changing the temperature of said sample until the majority of said sample is at the final temperature," is performed.

Uniformity may be achieved according to, for example, the methods disclosed at page 8, line 5 to page 9, line 14 of the present specification.

In this regard, uniformity may be achieved, for example, by:

- (a) placing the sample in a region with the intermediate temperature, the region having a pre-determined length along the direction of the movement of the sample, the length of this region potentially being shorter than the sample, such that it would allow the sample, while being moved along the region, to have the leading end reach the intermediate temperature by the time the

same leading end leaves the region;

- (b) placing the sample in a region with the intermediate temperature, the region having a pre-determined length along the direction of the movement of the sample, the length of this region may be substantially equal to or greater than the length of the sample along the direction of its movement.; or
- (c) moving the sample into the region with the intermediate temperature, until substantially the whole sample is within said region; pausing the movement of the sample within said region until the temperature of the sample is substantially uniform throughout the sample and equals the intermediate temperature, and moving the sample out of this region.

With regard to (a), the remainder of the sample will thus be subjected to the intermediate temperature until the temperature of this remainder also equals the intermediate temperature. Therefore, since the sample is exposed simultaneously to more than one region, the velocity of movement in all regions must be the same, to allow each and every part of the sample to undergo substantially the same thawing or freezing process.

With reference to each of the pending independent claims and in regards to (b) above, Applicants note that the sample is moved in the region according to step (i) and into the region of step (ii) with one velocity. The sample is then moved from the region of step (ii) and through the region of step (iii) at another velocity. Accordingly, the velocity of movement in step (ii) would be variable, at least in the range between the velocities of

movement in steps (i) and (iii).

In contrast to the presently claimed subject matter, Applicants submit that the '254 patent does not teach or suggest either ***providing said biological matter in the form of a sample whose minimal dimension in each of two mutually perpendicular cross-sections exceeds 0.5 centimeters, and at least one of the cross-sections having an outer zone and an inner zone such that the temperature of the sample in the outer zone changes quicker than that in the inner zone or further changing the temperature of said sample by subjecting it to the intermediate temperature until the temperature of said sample in at least one cross-section is uniform and equals the intermediate temperature.*** See claims 78 and 121-123.

Applicants respectfully reiterate that the present subject matter differs from that of the '254 patent for at least the reason that in contradiction to the essentially simultaneous (or at least very quick) temperature change between outer and inner zones of a small sample as taught in the '254 patent, the temperature of a large sample does not change uniformly when the entire sample is subjected to a temperature different than that of the sample. Therefore, ***the presently claimed subject matter is not a merely a scaling up the process of the '254 patent.*** In other words, due to small height of the sample of the '254 patent, the speed of temperature change realized in any cross-section of the outer and inner zones of the sample is essentially the same. Therefore, the '254 patent does not teach or suggest subjecting a sample to an intermediate temperature ***until the temperature of the sample in said cross-section is uniform*** and equals the

intermediate temperature.

In view of the foregoing, it is submitted that nothing in the '254 patent renders the presently claimed subject matter obvious within the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

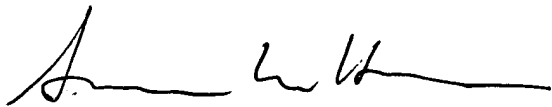
CONCLUSION

Applicants assert that the claims are in condition for immediate allowance and early notice to that effect is earnestly solicited. Should the Examiner deem that any further action by Applicants' undersigned representative is desirable and/or necessary, the Examiner is invited to telephone the undersigned at the number set forth below.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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